For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

UNISPEED-CZ

1. Generic Name

Ascorbic Acid (Vitamin C) and Zinc Chewable Tablets

2. Qualitative and quantitative composition

Each uncoated chewable tablet contains:

Ascorbic Acid I.P 100mg

Sodium Ascorbate I.P.....450mg

Equivalent to Ascorbic Acid… 400mg

Zinc Citrate NF Equivalent to elemental Zinc ... 5mg

Excipients .....qs

Colour: Sunset Yellow FCF

The excipients used are Sucrose, Tartaric Acid, Saccharin, Colour Sunset Yellow,

Magnesium Stearate, Flavour Trusil Orange and Flavour Trusil Pineapple.

3. Dosage form and strength

Dosage Form: Uncoated Chewable tablets

Strength: 500mg/5mg

4. Clinical particulars

4.1 Therapeutic indication

UNISPEED-CZ chewable tablets are indicated for the prevention and treatment of ascorbic acid (Vitamin C) and zinc deficiency if sufficient supply from the diet is not ensured.

4.2 Posology and method of administration

Posology

Dosage should be as directed by the Physician.

Method of administration

Tablets should be taken orally. Tablets are to be chewed before swallowing. Do not swallow whole tablet.

4.3 Contraindications

- Hypersensitivity to the active ingredient or any of the other constituents.
- Oxalate urolithiasis and iron storage diseases (thalassaemia, haemochromatosis, sideroblastic anaemia) or other medical conditions that predispose individuals to iron overload.
- Patients suffering from or having a history of Nephrolitiasis must not take this product.

- Patients suffering from severe renal insufficiency or renal failure must not take the product. This includes patients on dialysis.

4.4 Special warnings and precautions for use

Exceeding the recommended dose should be avoided as there have been isolated reports of severe haemolysis in patients with erythrocytic glucose-6-phosphate dehydrogenase deficiency when taking high doses (> 4000 mg/day) of ascorbic acid. Do not exceed the recommended dose.

Patients suffering from glucose-6-phosphatase deficiency should not take higher than the recommended dose. Overdose of Ascorbic acid in this patient population has been associated with haemolytic anaemia.

Caution is required and use the minimum recommended dose in patients with renal impairment. Patients suffering from renal insufficiency should consult a physician or healthcare professional prior to intake of large doses.

Patients with rare hereditary fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase deficiency should not take ascorbic acid.

Patients receiving other single vitamins or multivitamin preparations, any other medication or those under medical care must consult a health care professional before taking this product.

Ascorbic acid may interfere with laboratory tests resulting in false readings. Inform your physician when taking this product and diagnostic measures are planned or done. Ascorbic acid may interfere with test kits and meters measuring glucose levels resulting in false results. Please check the package insert of the test kit or meter for guidance.

Keep out of sight and reach of children.

4.5 Drugs interactions

<u>Ascorbic Acid</u>

Administration of ascorbic acid leads to increased absorption of iron from the gastrointestinal tract. This should be borne in mind in the case of iron replacement.

Concurrent administration of ascorbic acid with deferoxamine enhances urinary iron excretion.

Cases of cardiomyopathy and congestive heart failure have been reported in patients with idiopathic haemochromatosis and thalassaemias receiving deferoxamine who were subsequently given ascorbic acid. In early treatment, when there is excess tissue iron, there is some evidence that ascorbic acid may worsen iron toxicity, particularly to the heart.

Ascorbic acid may increase gastrointestinal absorption of aluminium. Concomitant administration of aluminium-containing antacids may affect urinary aluminium elimination. Concurrent administration of antacids and ascorbic acid is not recommended, especially in patients with renal insufficiency.

Ascorbic acid may reduce cyclosporine blood levels.

High doses of Ascorbic acid may interfere with the effectiveness of warfarin.

Lab test interactions:

As Ascorbic acid is a strong reducing agent, it can cause chemical interference in laboratory tests that involve oxidation-reduction reactions, such as the analyses of glucose, creatinine, carbamazepine, uric acid, and inorganic phosphates in urine, serum and of occult blood in faeces. Refer to the manufacturer's information to determine if Ascorbic acid interferes with the test.

Zinc:

Zinc forms complexes with certain substances (including tetracycline antibiotics, quinonolone antibiotics, penicillamine) resulting in decreased absorption of both substances. As these interactions occur in the gastro-intestinal tract, the potential for interaction should be reduced by taking the product separately from other drugs. It is usually sufficient to separate the intake by at least 2 hours before or 4-6 hours after ingestion of the other drug, unless otherwise specified.

Zinc may reduce copper absorption.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

The product is generally considered safe during pregnancy and lactation when used as labelled. However, since there are no sufficient controlled human studies assessing the risk of the product during pregnancy or lactation, the product should be administered in pregnancy or lactation only when clinically indicated and considered essential by the physician.

The recommended dose should not be exceeded as chronic overdose might be harmful to the foetus and neonate. Ascorbic acid and Zinc are secreted into breast milk. This must be taken into consideration if the infant is receiving any other supplements.

Neither non-clinical nor clinical data are available to assess aspartame use in infants below 12 weeks of age.

Fertility

To date, there is no evidence suggestive that Ascorbic acid and/or zinc causes adverse reproductive effects in humans.

4.7 Effects on ability to drive and use machines

The product has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions reported from post-marketing experience are tabulated below by System Organ Class and frequency. The following convention has been utilised for the classification of undesirable effects:

Very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000,<1/100), rare (≥1/10,000, <1/1000), very rare (<1/10,000), not known (cannot be estimated from available data).

Immune system disorders

Very rare: Allergic reactions, including hypersensitivity reactions (such as shortness of breath, swelling of the face and skin rash).

Nervous system disorders

Very rare: Headache and dizziness.

Gastrointestinal disorders

Very rare: Nausea, vomiting, diarrhoea, dyspepsia and abdominal pain.

General disorders and administration site conditions

Very rare: Fatigue

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

https://torrentpharma.com/index.php/site/info/adverse_event_reporting.

4.9 Overdose

Clinical signs and symptoms, laboratory findings, and consequences of overdose are highly diverse, dependent on an individual's susceptibility and surrounding circumstances.

General manifestations of overdose with Ascorbic acid and/or zinc may include increase of gastrointestinal disturbances including diarrhea, nausea, and vomiting. Occasionally transient osmotic diarrhoea may occur in doses over 3 g and almost always at doses above 10 g.

If such symptoms occur, the product should be stopped and a healthcare professional consulted.

Specific clinical manifestations may include the following*:*

Ascorbic acid:
Acute or chronic overdose of Ascorbic acid may significantly elevate serum and urinary oxalate levels. In some instances, this may lead to hyperoxaluria, calcium oxalate crystalluria, calcium oxalate deposition, kidney stone formation, tubulointerstitial nephropathy, and acute renal failure. Individuals with mild to moderate renal insufficiency may be susceptible to these effects of Ascorbic acid toxicity at lower doses and should consult a health care professional before use of the product. Overdose of Ascorbic acid may result in oxidative hemolysis or disseminated
intravascular coagulation in patients with glucose-6-phosphate dehydrogenase deficiency.

Zinc:
Zinc overdose can cause irritation and corrosion of the gastrointestinal (GI) tract, acute renal tubular necrosis, interstitial nephritis, copper deficiency, sideroblastic anemia, and myeloneuropathies.
If overdose with the product is suspected, intake should be stopped and a health care professional consulted for treatment of clinical manifestations. Ascorbic acid is removed by hemodialysis.

5. Pharmacological properties

5.1 Mechanism of Action

Ascorbic acid is an electron donor (reducing agent or antioxidant), and probably all of its biochemical and molecular functions can be accounted for by this function.

The body requires zinc to develop and activate T-lymphocytes. Zinc is also required for macrophage and neutrophil functions, natural killer cell activity, and complement activity. Zinc helps maintain the integrity of skin and mucosal membranes

5.2 Pharmacodynamic properties

Vitamin C and zinc are required to support the functions of innate immunity, such as epithelial barriers and the cellular components involved in phagocytosis. While vitamin C and zinc both support epithelial barriers, although by different mechanisms, they target different populations of phagocytic cells, thereby complementing each other to ensure an effective phagocytic response.

Among the micronutrients required to ensure proper immune function, vitamin C and zinc play a central role through their complementary roles in supporting components of both innate and adaptive immunity, such as epithelial barriers, cellular proliferation and antibody production. Vitamin C and Zinc provide complementary antioxidant protection to exogenously derived and endogenously generated ROS (reactive oxygen species).

Ascorbic acid:

Due to its redox potential ascorbic acid acts as a co-factor of numerous enzyme systems (collagen formation, catecholamine synthesis, hydroxylation of steroids, tyrosine and exogenous substances, biosynthesis of carnitine, regeneration of tetrahydrofolic acid and alphaamidation of peptides, e.g. ACTH and gastrin). In addition a ascorbic acid deficiency impairs the immune defence reactions, especially chemotaxis, complement activation and interferon production. The molecular biological functions of ascorbic acid have not been fully elucidated. Ascorbic acid improves the absorption of iron salts by reducing ferric ions and forming iron chelates. It blocks the chain reactions triggered by oxygen radicals in aqueous compartments of the body. The antioxidative functions form a close biochemical interaction with those of vitamin E, vitamin A and carotenoids.

Zinc:

Zinc is a key trace mineral, involved in many biological processes. Zinc is necessary for basic cell activities such as cell growth, differentiation, and survival. It plays vital role in both the innate and acquired including immunity. Zinc deficiency reduces lymphocyte counts and impairs their function.

Zinc status is of major importance in maintenance of effective immune response, particularly T-cell-mediated response. Zinc functions as an antioxidant and has anti-inflammatory actions. Zinc supplementation decreases oxidative stress markers and generation of inflammatory cytokines.

5.3 Pharmacokinetic properties

Absorption and Excretion:

Ascorbic acid is absorbed primarily in the upper part of the small intestine via sodium-dependent active transport. When ascorbic acid is present in high concentrations, uptake occurs by means of passive diffusion. After oral administration of doses of 1-12 g, the proportion of

ascorbic acid absorbed falls from approximately 50% to about 15%, though the absolute quantity of substance taken up continues to increase.

Zinc is absorbed all along the small intestine. The absorption of zinc (ionic) administered in solution on an empty stomach ranges from 41-79%, while the zinc present in foods or that given as a supplement with meals is absorbed in the range of 10–40%.

Distribution:

The physiological body pool of Ascorbic acid is about 1500 mg. Plasma protein binding of ascorbic acid is approximately 24%. Serum concentrations are normally 10 mg/l (60 µmol/l). Concentrations below 6 mg/l (35 µmol/l) indicate that the intake of Ascorbic acid is not always adequate, and concentrations below 4 mg/l (20 µmol/l) indicate that the intake is actually inadequate. In clinically manifest scurvy, serum concentrations are below 2 mg/l (10 µmol/l).

Total body zinc content is controlled in part by regulating the efficiency of intestinal absorption and the excretion from endogenous zinc pools to maintain zinc homeostasis. The adult total body zinc content ranges from about 2.3 mmol (1.5 g) in women to 3.8 mmol (2.5 g) in men. Zinc is present in all organs, tissues, fluids, and secretions of the body. Zinc is primarily an intracellular ion, with well over 95% of the total-body zinc found within cells. Zinc is associated with all organelles of the cell, but about 60 to 80% of the cellular zinc is found in the cytosol.

Metabolism:

Ascorbic acid is metabolised partly via dehydroascorbic acid to oxalic acid and other products. When ingested in excessive quantities, however, ascorbic acid is largely excreted in unchanged form in the urine and faeces. Ascorbic-acid-2-sulphate also appears as a metabolite in the urine.

The total amount of zinc present in the major tissues is much larger than the total in plasma. Thus, relatively small variations in zinc content of tissues, such as the liver, can have dramatic effects on the plasma zinc. All absorbed zinc passes through the plasma to the tissues, and the flux of zinc through the plasma is said to be replaced approximately 130 times per day. There is no specific zinc "store". Human experimental studies with low-zinc diets 2.6-3.6 mg/day /40-55 mmol/day) haveshown that circulating zinc levels and activities of zinc-containing enzymes can be maintained within normal range over several months highlighting the efficiency of the zinc homeostasis mechanism.

Elimination:

The physiological body pool of ascorbic acid is about 1500 mg. The elimination half-life of ascorbic acid depends on the route of administration, the quantity administered and the rate of absorption. Following an oral dose of 1 g the half-life is about 13 hours. When 1-3 g Ascorbic acid /day is taken, the main route of excretion is renal. With doses exceeding 3 g, increasing quantities are excreted unchanged in the faeces.

The major route for endogenous zinc excretion is into the gastrointestinal tract with ultimate loss in the faeces. When tracer doses of zinc are given either orally or intravenously, only about 2 to 10% is recovered in the urine; the remainder is lost in the faeces. In humans, endogenous faecal losses may range from <15 µmol/day (1 mg/day) with extremely low intakes to over 80 µmol/day (5 mg/day) with extremely high intakes. Normally, about 6 to 9 µmol (400 to 600 µg) of zinc is excreted daily in the urine.

Patients with G6PD deficiency:

Large doses of ascorbic acid are reported to result in haemolysis in patients with G6PD deficiency.

6. Nonclinical properties

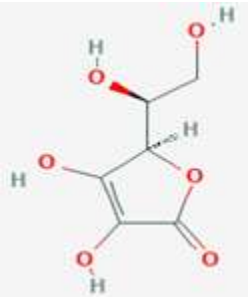
6.1 Animal Toxicology or Pharmacology

No specific study with this product was done, but the preclinical safety of the individual components has been extensively documented.

7. Description

Ascorbic Acid

Ascorbic Acid is a natural water-soluble vitamin (Vitamin C). It is chemically, (2R)-2-[(1S)-1,2-dihydroxyethyl]-3,4-dihydroxy-2H-furan-5-one having molecular formula of $C_6H_8O_6$ and molecular weight of 176.12g/mol. The chemical structure is:



Zinc:

Zinc is an essential mineral and heavy metal that is included in most over-the-counter multivitamin and mineral supplements. The molecular formula is Zn and molecular weight is 65.4g/mol.

UNISPEED-CZ

Ascorbic Acid and Zinc Chewable Tablets light are orange to orange coloured mottled, round shaped, flat faced, beveled edge, uncoated chewable tablets with breakline on one side and plain on other side. The excipients used are Sucrose, Tartaric Acid, Saccharin, Colour Sunset Yellow, Magnesium Stearate, Flavour Trusil Orange and Flavour Trusil Pineapple.

8. Pharmaceutical particulars

8.1 Incompatibilities

None stated

8.1 Shelf-life

Do not use later than the date of expiry.

8.2 Packaging information

UNISPEED-CZ is available in strip of 15 tablets.

8.3 Storage and handing instructions

Store at a temperature not exceeding 25°C. Protect from light and moisture.

9. Patient counselling information

UNISPEED-CZ Tablets

Ascorbic Acid (Vitamin C) and Zinc Chewable Tablets

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- Keep all medicines out of reach of children
- If you have any further questions, ask your doctor or pharmacist.
- **This medicine has been prescribed for you only.** Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet?

9.1 What UNISPEED-CZ is and what it is used for

- UNISPEED-CZ are a vitamin and mineral supplement containing Ascorbic acid and zinc. UNISPEED-CZ are for the treatment of Ascorbic acid and zinc deficiency)

9.2 What you need to know before you take UNISPEED-CZ

Do not take UNISPEED-CZ

- If you are allergic to Ascorbic acid or zinc or any of the other ingredients.
- If you suffer or suffered from kidney stones, or have high oxalic levels in the urine.
- If you have severe problems with your kidneys or are on dialysis.
- If you suffer from iron overload (hemochromatosis).

Warnings and precautions

- If you have been told that you have a rare genetic disease causing a deficiency of glucose-6-phosphate dehydrogenase.
- If you are prone to kidney stones, use caution with high dose Ascorbic acid formulations.
- Please consult your doctor or pharmacist before taking UNISPEED-CZ if you have any kidney problems. Ascorbic acid should not be taken in higher doses, or for longer than recommended, as overdose may lead to kidney problems.
- Diabetics: Ascorbic acid can interfere with some test kits used to determine blood sugar content. It has no effect on blood sugar levels. Ask your doctor or pharmacist if your test result can be affected by taking vitamin supplements.

- If your doctor recommends that you have any hospital tests, mention to him that you are taking UNISPEED-CZ, this is because Ascorbic acid may interfere with some tests.

Other medicines and UNISPEED-CZ

Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines including those obtained without a prescription or any vitamin supplements.

Driving and using machines

It has not been established that UNISPEED-CZ impairs your ability to drive or operate any tools or machinery. However, you should not drive or use machines until it is established that your ability to perform such activities is not affected.

9.3 How to take UNISPEED-CZ

Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist have told you. Check with your doctor or pharmacist if you are not sure.

Tablets should be taken orally. Tablets are to be chewed before swallowing. Do not swallow whole tablet.

If you take more UNISPEED-CZ than you should

Contact your doctor if you took more doses than you should. Your doctor will establish the best possible treatment of overdose.

If you forget to take UNISPEED-CZ:

Contact your doctor if you have missed one or more doses.

Do not take a double dose to make up for a forgotten dose.

If you stop taking UNISPEED-CZ

Should your doctor decide to stop your UNISPEED-CZ treatment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor immediately or contact the casualty department at your nearest hospital, if you get any of the following serious side effects:

Difficulty in breathing or swallowing, swelling of the face, lips, throat or tongue, skin rashes, large or itchy wheals on the skin, attacks of sneezing, runny nose and itching eyes or water retention.

Other side effects: Headache, dizziness, nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, Fatigue.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

https://torrentpharma.com/index.php/site/info/adverse_event_reporting. By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store UNISPEED-CZ

Store at a temperature not exceeding 25°C. Protect from light and moisture.

9.6 Contents of the pack and other information

What **UNISPEED-CZ** contains

The active substances are Ascorbic acid (Vitamin C) and Zinc.

Ascorbic Acid I.P..... 500mg

Elemental Zinc 5mg

Other ingredients are Sucrose, Tartaric Acid, Saccharin, Colour Sunset Yellow, Magnesium Stearate, Flavour Trusil Orange and Flavour Trusil Pineapple.

10. Details of manufacturer

Exemed Pharmaceuticals

Plot No. 133/1 and 133/2, G.I.D.C., Selvas Road, Vapi – 396195, Dist. Valsad, Gujarat, India.

11. Details of permission or licence number with date

Mfg Lic No. G/28/1455 issued on 06.11.2020

12. Date of revision

Not Applicable

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/UNISPEED-CZ, 500mg, 5mg/DEC-20/01/PI